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Complaints about impairments in executive functions in Parkinson's disease: The association with neuropsychological assessment

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ABSTRACT

Impairments in executive functions are frequently reported in Parkinson's disease (PD). However, little is known about patients' experience regarding these impairments. This knowledge is crucial because if patients do not experience their cognitive impairments they do not report them to their attending neurologist. Consequently, patients might not get appropriate treatment. This study investigated if patients with a mild to moderate PD experience impairments in executive functions in daily life and whether these correspond with impairments as measured in neuropsychological assessments.

Forty-three PD patients and 25 healthy participants were included. Groups did not differ in age, sex and education. All participants and their closest relatives completed a standardized questionnaire measuring executive functions in daily life. Furthermore, all participants were assessed with a test battery measuring executive functions.

PD patients reported significantly more problems with executive functions in daily life than healthy participants. Furthermore, co-morbid depression had a negative impact on the number of problems with executive functions in daily life as reported by PD patients. The experienced daily life problems in executive functions were not associated with the patients' performance on objective cognitive measures.

In conclusion, PD patients were aware of problems with executive functions in daily life and reported considerably more problems than healthy controls. These problems were however not reflected by neuropsychological tests and may indicate a lack of ecological validity of neuropsychological assessment.

1. Introduction

An important issue in the assessment of neurological patients is the accuracy with which patients can rate the cognitive impairments they encounter in daily life. A problem that often occurs, however, is that not all patients with cognitive impairments complain about their cognitive limitations [1,2]. To overcome this problem, neuropsychological assessment procedures are used. However, the standard tests used in these assessments do not always reflect daily life cognitive impairments [3,4].

Parkinson's disease (PD) is a neurological disorder in which cognitive impairments are apparent, in particular in the domain of executive functions [5], and only little is known about to what extent patients experience their cognitive limitations. The few studies that focused on the complaints of PD patients with regard to their cognitive impairments are characterized by methodological limitations (e.g. lack of concurrent validity of test measures applied) and inconsistent results [6–8]. Since complaints about cognitive limitations have a negative impact on caregivers' stress and influence the willingness of patients to seek or to comply with treatment [9,10], knowledge about PD patients' experience of cognitive limitations appears crucial. In addition, it is important to determine whether manifestations of cognitive limitations in daily life as reported by PD patients correspond with impairments found in neuropsychological assessments. This knowledge might provide an insight in the accuracy of patients' self-reports but also in the ecological validity of neuropsychological tests. The current study aimed to determine if patients with a mild to moderate PD experience impairments in executive functions in daily life and whether these are associated with both evaluations of relatives and the results of neuropsychological measurements.

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2. Methods

2.1. Participants

Forty-three PD patients participated in this study. All patients were recruited from the Movement Disorders outpatient clinic of the Department of Neurology of the University Medical Center Groningen (UMCG), The Netherlands, and were diagnosed with idiopathic PD according to the criteria of the UK Parkinson's Disease Society Brain Bank. The motor severity of symptoms was assessed with the Unified Parkinson's Disease Rating Scale and Hoehn and Yahr scale (H&Y). A Levodopa Equivalent Daily Dose (LEDD) was calculated for all patients [11]. All patients were assessed in their regular on-state of medication. In addition, 25 healthy participants were included in this study. Level of education was rated for all participants with a Dutch education scale, ranging from 1 (elementary school not finished) to 7 (university degree). Groups did not differ in age ($t = 0.35$; $p =$ not significant; ns), gender (Chi-Square = 0.88; $p =$ ns) and education level ($Z = -1.58$; $p =$ ns). Descriptive and disease characteristics of PD patients and healthy participants are reported in Table 1. Patients with dementia (MMSE < 24) and neurological disorders other than PD were excluded. This study was approved by the medical ethical committee of the UMCG. All participants signed an informed consent prior to study inclusion.

2.2. Stimulus material

2.2.1. Executive functions in daily life

The *Dysexecutive questionnaire* (DEX) [12] is a sensitive instrument with an adequate concurrent validity [13]. It consists of 20 questions that cover the most commonly reported symptoms of the dysexecutive syndrome. Participants are asked to rate on a scale that ranges from 0 (never) to 4 (very often) how often they observed the symptoms described in the DEX (*DEX self*). Furthermore, a close relative of the participant was also asked to complete the DEX and to rate how often they observed the symptoms of the dysexecutive syndrome in their relative (*DEX other*). For both the *DEX self* and the *DEX other* a total score was calculated.

2.2.2. Neuropsychological test measures of executive functions

Several standardized, reliable and valid neuropsychological test measures of executive functions were applied in this study [14]. The *Stroop Color Word Test* [15] was used to measure inhibition. Cognitive flexibility was assessed with the *Trail Making Test* [16] and the *Odd Man Out* [17]. The *Digit Span* of the Wechsler Memory Scale–Revised [18] was used to assess working memory. *Semantic and phonemic verbal fluency tests* were used to evaluate divergent thinking. Finally, the *Zoo-Map* of the Behavioral Assessment of the Dysexecutive Syndrome [19] was used to assess planning.

2.3. Statistical analyses

Normality of data was analyzed, using the Shapiro–Wilk test and QQ-plots. While the *DEX self* and *DEX other* were normally distributed, neuropsychological test measures of executive functions were not. Therefore, parametric tests were used when comparing the performance of groups on the *DEX self* and *DEX other*. Non-parametric tests were used when comparing the test performances of groups or when calculating associations between test performances and the *DEX self* and *DEX other*.

T-tests for independent samples were used to compare the performance of PD patients and healthy participants on the *DEX self* and *DEX other*. The Mann–Withney U test was used to compare the performance of groups on tests of executive functions. To determine the associations between the scores on the *DEX self*, *DEX other* and test performances, Spearman correlations were calculated. Furthermore, to determine whether the rating of participants corresponded with the rating of their relatives, the scores on the *DEX self* were compared with the scores on the *DEX other* within each group using related samples *t*-test.

Besides comparing PD patients to healthy participants, the rating of PD patients in H&Y stage 1–2 on the *DEX self* and *DEX other* were compared to PD patients in H&Y stage 2.5–3. PD patients in H&Y stage 2.5–3 had a significantly higher age ($t = -3.0$; $p = 0.005$) and a significantly lower level of education ($z = -2.4$; $p = 0.02$) than PD patients in H&Y stage 1–2. Both groups were comparable with regard to gender (Chi-Square = 3.6; $p =$ ns). Therefore, a MANCOVA was used to compare the ratings on the *DEX self* and *DEX other* of PD patients in H&Y stage 1–2 and PD patients in H&Y stage 2.5–3, including age and education as covariates. Also, within these groups the *DEX self* was compared to the *DEX other* using related samples *t*-tests. Since a (M)ANCOVA is robust against deviations from normality [20], this test was also used for comparison of test performance between PD patients in H&Y stage 1–2 and PD patients in H&Y stage 2.5–3 with age and education as covariates. All these calculations were also performed with the groups of PD patients with co-morbid depression (MADRS score ≥ 18; [21]) and PD patients without depression (MADRS score < 18; [21]). However, since PD patients with co-morbid depression and PD patients without depression did not differ regarding age ($t = -1.1$; $p =$ ns), education ($z = 1.0$; $p =$ ns) and gender (Chi-Square = 0.1; $p =$ ns) *t*-tests and Mann–Withney U tests were used for data analyses. Finally, Cohen's d was calculated for all comparisons. The threshold for statistical significance was 0.05.

Table 1
Descriptive and disease characteristics of PD patients ($n = 43$) and healthy participants ($n = 25$).

	PD patients	Healthy participants
	M (SD)	M (SD)
Age (years)	63.7 (8.6)	62.8 (11.5)
Education[a]	5.2 (1.1)	4.8 (0.7)
Gender		
Male: *n* (%)	24 (56)	11 (44)
Female: *n* (%)	19 (44)	14 (56)
MADRS total	9.2 (7.1)	2.3 (2.1)
MMSE total	27.5 (1.4)	27.6 (1.2)
Disease duration (years)	5.1 (4.1)	
UPDRS, part III	24.6 (8.8)	
H&Y	2.2 (0.6)	
LEDD	561.7 (435.3)	

MADRS = Montgomery-Åsberg Depression Rating Scale; MMSE = Mini Mental State Examination; UPDRS = Unified Parkinson's Disease Rating Scale; H&Y = Hoehn and Yahr scale; LEDD = Levodopa Equivalent Daily Dose.

[a] Dutch education scale ranging from 1 (elementary school not finished) to 7 (university degree).

3. Results

3.1. Comparison of PD patients and healthy participants

PD patients showed significantly higher scores on the *DEX self* compared to healthy participants ($t = 2.1$; $p = 0.04$; $d = 0.5$). No differences were found between these groups for the *DEX other* ($t = 1.9$; $p =$ ns; $d = 0.4$; Fig. 1a). In PD patients, 58% of 'relatives' were partners, 19% children, 12% close friends or family members. In 11% of cases the type of relationship was unknown. All 'relatives' were caregivers of patients. In the group of healthy participants, 44% of the 'relatives' were partners, 12% children and 28% close friends or family members. In 16% of cases the type of relationship was unknown. PD patients and healthy participants reported on average the same number of problems as their relatives (respectively, $t = -1.6$; $p =$ ns; $d = 0.2$ and $t = -1.6$; $p =$ ns; $d = 0.5$; Fig. 1a). PD patients also showed significantly lower scores on tests of executive functions than healthy participants (Table 2). However, only weak non-significant associations were found between the *DEX self*, *DEX other* and the test performances of PD patients (correlations ranging from respectively −0.13 to 0.18, and from −0.17 to 0.13).

3.2. Comparison of PD patients in H&Y stage 1–2 and PD patients in H&Y stage 2.5–3

The DEX scores of patients in H&Y stage 1–2 were compared to the scores of patients in H&Y stage 2.5–3, with a correction for age and education. No differences were found between these groups with regard to *DEX self* ($F = 1.9$; $p =$ ns; $d = 0.4$) and *DEX other* ($F = 0.91$; $p =$ ns; $d = 0.2$; Fig. 1b). However, the *DEX self* differed significantly from the *DEX other* within PD patients in H&Y stage 2.5–3 ($t = -3.6$; $p = 0.002$; $d = 0.6$). This difference was not found within PD patients in H&Y stage 1–2 ($t = 0.3$; $p =$ ns; $d = 0.1$; Fig. 1b). In neuropsychological assessment, no significant differences were found between the two groups (F-scores ranging from 0.01 to 0.89; *p*-values ranging from 0.35 to 0.98; data not shown).

3.3. Comparison of PD patients with co-morbid depression and PD patients without depression

PD patients with depression scored significantly higher on the *DEX self* ($t = -3.4$; $p = 0.001$; $d = 1.4$) and *DEX other* ($t = -2.3$; $p = 0.02$; $d = 0.9$) compared to PD patients without depression

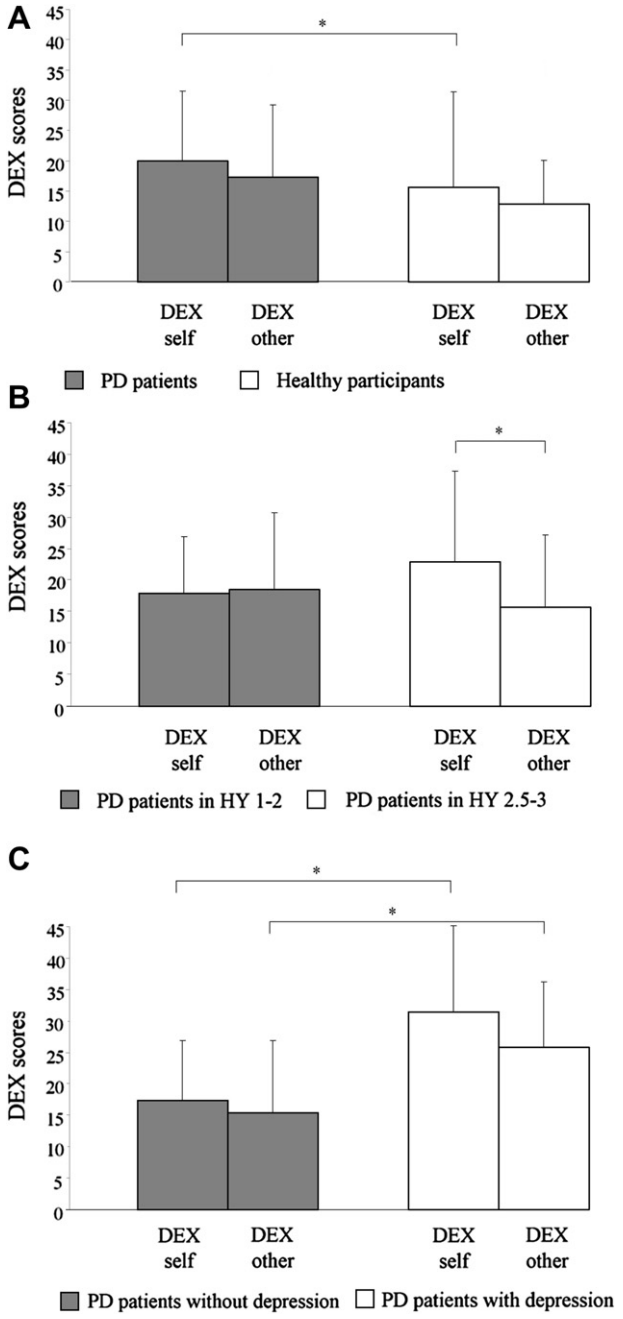

Fig. 1. Dysexecutive questionnaire (DEX): a. Scores of PD patients ($n = 45$) and healthy participants ($n = 25$) on the DEX (Mean ± SD), *$p < 0.05$. b. Scores of PD patients in different stages of the disease on the DEX (Mean ± SD; HY1-2 $n = 25$; HY 2.5–3 $n = 18$), *$p < 0.05$. c. DEX scores of PD patients with ($n = 8$) and without depression ($n = 35$; Mean ± SD), *$p < 0.05$.

(Fig. 1c). Furthermore, PD patients with and without depression reported on average the same number of problems as their relatives (respectively, $t = 1.1$; $p =$ ns; $d = 0.5$; $t = 1.5$; $p =$ ns; $d = 0.2$). PD patients with depression did, however, not differ in tests measuring executive functions from PD patients without depression (z-scores ranging from −0.4 to −0.7; p-values ranging from 0.50 to 0.97; data not shown).

4. Discussion

PD patients reported significantly more problems with executive functions in daily life than healthy participants. Furthermore, there was agreement between PD patients and their relatives with regard to the problems patients encounter in daily life, which suggests that PD patients have a good insight into their daily life functioning. This is the first study to report that PD patients are aware of impairments in executive functions in daily life and experience more problems than healthy elderly people. These results are in line with studies reporting that PD patients and their relatives are aware of several other non-motor symptoms [22].

Table 2
Performance of PD patients ($n = 43$) and healthy participants ($n = 25$) on tests for executive functions (two-tailed).

	PD patients	Healthy participants	z	p
	M (SD)	M (SD)		
Inhibition				
Stroop interference index	1.7 (0.4)	1.6 (0.2)	−1.2	ns
Cognitive flexibility				
TMT B	126.0 (57.3)	102.6 (68.4)	−2.5	0.01**
OMO no errors	5.4 (5.9)	1.2 (1.4)	−3.5	<0.001**
Word fluency				
Fluency animals	21.1 (5.2)	21.6 (4.4)	−0.5	ns
Fluency professions	15.2 (4.2)	17.5 (3.8)	−2.2	0.03*
Fluency letters	38.3 (15.4)	38.7 (10.5)	−0.6	ns
Working memory				
WAIS digit span backwards	5.7 (2.1)	6.1 (1.4)	−1.3	ns
Planning				
Zoo map	2.4 (1.2)	2.8 (0.9)	−1.4	ns

*$p \leq 0.05$; **$p \leq 0.01$.
TMT = Trail Making Test; OMO = Odd Man Out test; WAIS = Wechsler Adult Intelligence Scale; ns = not significant.

The problems with executive functions in daily life reported by PD patients did, however, not correspond with the neuropsychological assessment, even though PD patients showed an impaired performance on several tests of executive functions compared to healthy participants. Three possible explanations should be considered. First, neuropsychological tests do not always reflect executive impairments patients encounter in daily life (i.e. low ecological validity) [23]. This is possibly due to the fact that (classic) tests are usually very structured (rules and goals are set and start and end of behavior are prompted) [24–26]. However, situations in daily life are usually very unstructured, often without a clearly defined goal, solution, start and end. Furthermore, various approaches might be possible to solve a problem in daily life (e.g. planning a journey), while in standardized test procedures there is usually only one correct approach. Limitations in ecological validity of neuropsychological tests may thus account for the lack of an association between the problems reported by patients and neuropsychological assessment. Second, other tests (e.g. the CANTAB [27]) which are available to assess executive functions might be better related to day to day executive functions. A final explanation is that the DEX may not directly assess problems with executive functions in daily life but reflects the negative affect that accompanies the daily life problems with executive functions [28]. This latter explanation is consistent with the finding that depressed PD patients reported significant more problems with executive functions in daily life than non-depressed PD patients, even though no differences were found between these groups with regard to neuropsychological assessment. The influence of a negative mood on the subjective perception of cognitive impairments has previously been reported in PD [7] and in other neurological disorders [29,30]. A negative mood might thus adversely affect the rating of items of the DEX.

The agreement between PD patients and their relatives was, however, not the same in patients at different stages of the disease. Patients with mild PD reported on average the same number of problems with executive functions in daily life than their relatives. Patients with a moderate PD, on the other hand, reported on average more problems with executive functions in daily life than

their relatives. There might be two explanations for this finding. On the one hand, relatives of patients with moderate PD might not be fully aware of the daily life problems with executive functions patients might experience and may therefore underestimate these problems. Since patients with a moderate PD often have a relatively long disease duration, it is possible that their relatives became less sensitive over time and consequently report those problems less frequently. This is supported by the fact that patients with moderate PD did on average not report more problems than patients with mild PD. On the other hand, patients with moderate PD may overestimate problems with executive functions in daily life. Although it is possible that the insight of patients with a moderate PD into their daily life functioning is decreased it appears unlikely that this would result in an overestimation of problems. Research demonstrated that patients with frontal lobe pathology or neurodegenerative diseases are often indifferent to the consequences of their condition and therefore more likely to underestimate daily life problems [1].

A limitation of this study is the relative small group of PD patients with depression. However, even in this small group a significant difference was found between PD patients with and without depression in the number of problems with executive functions in daily life. Another limitation of this study is that no correction for multiple comparisons was performed. Important findings would have been lost because of the adjustment of the *p*-value. In this context, it has to be considered that the significant differences of the study are largely consistent with effect sizes, which were of medium to large size. Nevertheless, this is a weakness of the present study. In this context, the power of the study also has to be considered. Because of the sample sizes the power of analyses to detect a medium effect varied between 35% (e.g. patients with depression versus patients without depression) and 62% (e.g. PD patients versus healthy participants). Therefore, the results of some analyses should be viewed with caution. In future studies the findings of this study should be replicated.

In conclusion, PD patients are aware of their problems with executive functions in daily life and report considerably more problems than healthy controls. The problems patients experience in daily life did, however, not correspond with the results of neuropsychological assessment. These findings indicate that standard neuropsychological tests do not reflect the problems patients encounter in their everyday life and underline the need of ecologically valid neuropsychological tests. Finally, the present study indicates that a depressed mood has a detrimental effect on patients' self evaluations of executive functions in daily life.

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